

Easy Pathology

— Dr. Abdelrahman Khalifa —

Chapter 7

Neoplasm



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Neoplasia

Mass of cells, with uncontrolled, irreversible & unlimited proliferation

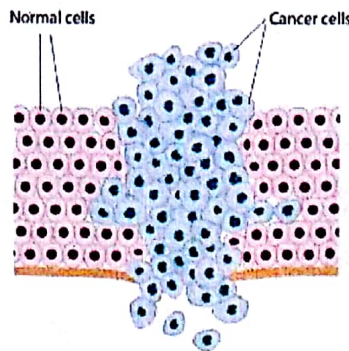
Classifications:

According to Behavior:

- Benign
- Malignant

According to Origin:

- Epithelial
- Mesenchymal
- Others



Microscopic features:

• Structure:

○ Parenchyma

- Epithelial tumors: acini, papillae, sheets, or cords
- mesenchymal tumors: Bundles, whorls with matrix (e.g. cartilage)
- some tumors show mixed pattern (e.g. pleomorphic adenoma, fibroadenoma, carcinosarcoma)

○ Stroma formed of:

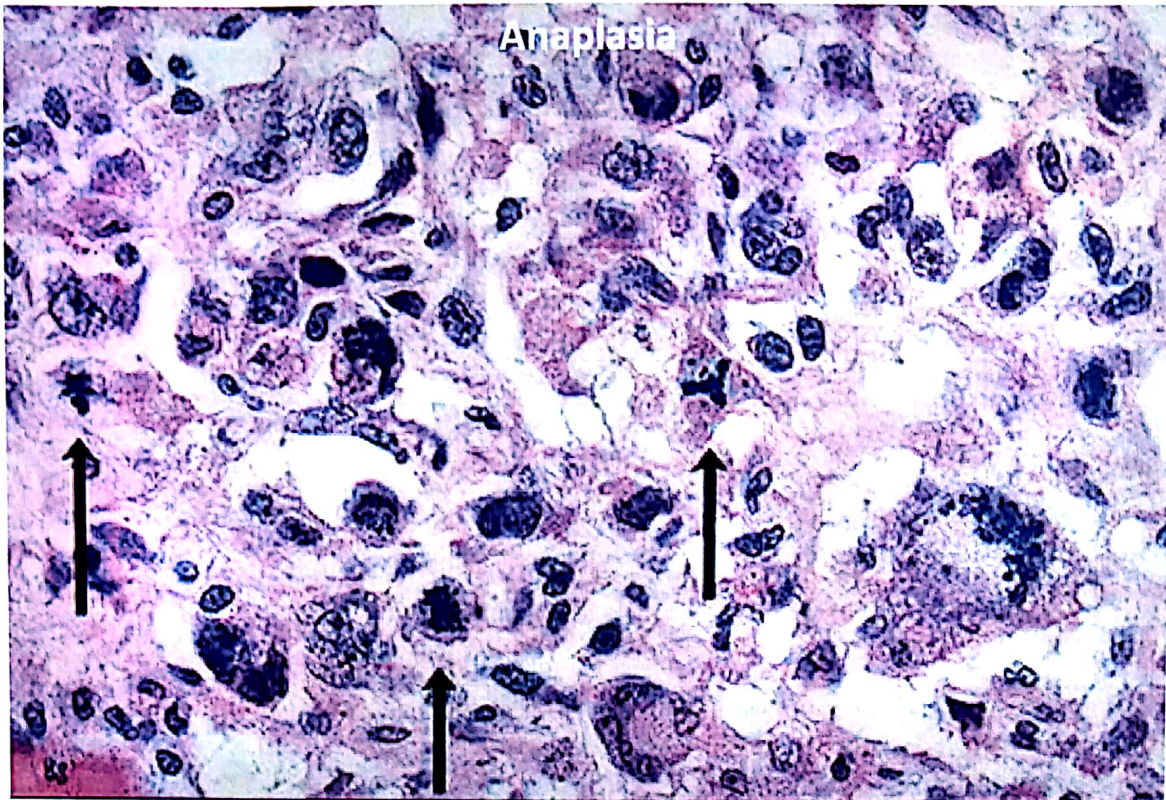
- Collagenous fibrous tissue
 - Stimulated by b-FGF
 - Scant stroma → gives fleshy consistency (e.g. sarcoma)
 - Excess (desmoplasia) → firm gritty (e.g. scirrhous carcinoma)
- Blood vessels (newly formed by Angiogenesis from preexisting ones)

• **Differentiation** similarity to origin. Variable according to type benign or malignant

• **Anaplasia** loss of differentiation, with morphological abnormality

- **Pleomorphism** *variable shape & size of tumor cells*
- **Hyperchromatism** *dark stained (increased nucleoprotein)*
- **Increased N/C ratio** $> 1:4$
- **Frequent mitoses & Abnormal mitotic figures** (*tripolar, multipolar*)
- **Abnormal nuclei (Anisonucleosis)** *vesicular, pleomorphic*
- **Prominent & multiple nucleoli**
- **Tumor giant cells**
- **Loss of polarity** *disturbed orientation and arrangement*
- **Functional Changes** (better differentiated tumors secrete hormone, bile or keratin)
- **Chromosomal changes** (*mutated genes & increased number of chromosomes* → large nucleus)

• **Inflammatory reaction** caused by 2ry infection of ulcer - or immune reaction against tumor (e.g. Inflammatory cells in Seminoma)



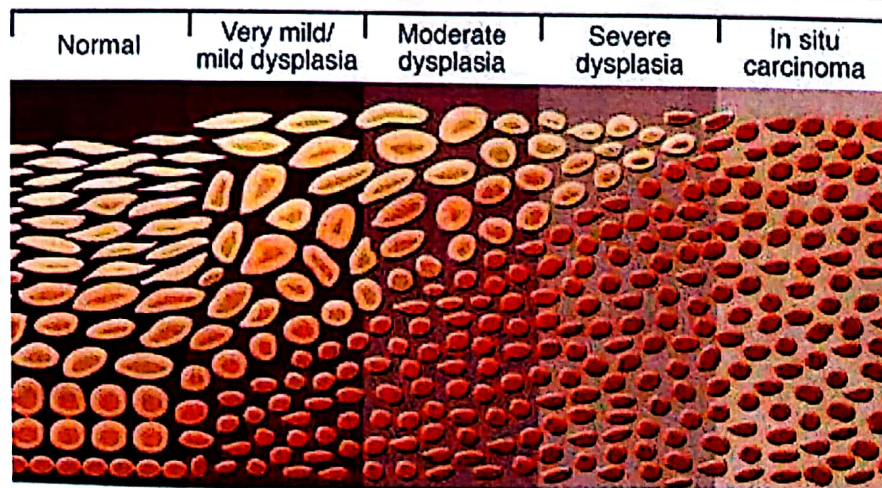
Dysplasia

Disordered arrangement and morphology of cells but not neoplastic
Site surface epithelium and glands_ caused by chronic irritation
Microscopic changes : _disorder of arrangement + Anaplasia (enumerate)

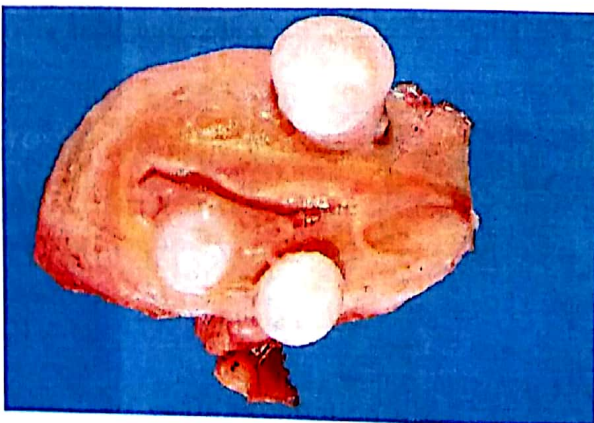
Grades of dysplasia in Stratified Squamous epithelium:

- **Grade I (mild)** : dysplasia of the lower third
- **Grade II (moderate)**: dysplasia of the lower 2/3
- **Grade III (severe)**: dysplasia of the full thickness → may change to Carcinoma in situ (CIS)

Fate: Dysplasia is precancerous but reversible



		Benign tumors	Malignant tumors
Behaviour	Rate of growth	Slow (could be <u>rapid</u> in <u>Leiomyoma</u> , which is hormonal-dependant) some tumors may <u>shrink</u> suddenly due to ischemia e.g. <u>pituitary adenoma</u>	Fast <u>Lead to central ischemic necrosis</u> -but Some tumors may shrink & disappear due to host immunity (e.g. <u>melanoma</u> , <u>choriocarcinoma</u>)
	Mode of growth	Expansion	Invasion and destruction
	Effect	Compression – obstruction – hormonal secretion	Same..... + effects of metastasis
	Spread & metastasis	Absent	present
	Recurrence	Not recurrent	Recurrent
	Prognosis	Good prognosis	Bad prognosis
Gross	Shape & boundaries	In solid organs: Rounded – oval surface epith.: papillae - polyp	In solid organs: irregular ill-defined surface epith.: fungating – ulcer-diffuse thickening
	Capsule	Capsulated Except <u>leiomyoma</u> , well-demarcated by compressed tissue (false capsule)	Not capsulated Some are partially capsulated (e.g. <u>follicular carcinoma</u> of thyroid)
	Surrounding tissue	compressed	infiltrated
Micro	Differentiation	Well differentiated	Variable well, moderate, poor, or undifferentiated
	Anaplasia	Absent	Present
	Chromosomal changes	Infrequent	Present



		Carcinoma	Sarcoma
origin		epithelial	mesenchymal
Behaviour	Rate of growth	Less Rapid	Rapid
	Mode of growth	infiltration	Infiltration and Expansion
	Spread	Early lymphatic → late blood	Early blood spread
	Prognosis	Relatively better	worse
	incidence	More common	Less common
	Age	Old age	Young age
Gross	Size	Relatively Smaller	Large bulky mass
	Shape	In solid organs: irregular ill-defined surface epith.: fungating – ulcer- diffuse thickening	irregular ill-defined
	C/S	Grayish white (better stroma) Less necrosis and hemorrhage.	Homogenous with extensive necrosis and hge.
	Consistency	Firm	Soft fleshy
Micro	Differentiation	More	Less
	Cohesion	More cohesive Arranged in sheets, glands, cords Separated by stroma	Less cohesive Highly cellular Individual cells
	Anaplasia	present	more
	Stroma	Less vascular Well formed fibrous stroma	highly vascular scant fibrous stroma

N.B. Malignant ulcer :

Raised everted edge – Necrotic hemorrhagic floor – Fixed indurated base



Methods of spread of Malignant tumors

- Benign tumor, Locally malignant tumors , & malignant brain tumors → No spread
- The more Anaplasia & tumor size → more likely is the spread
- 30% of malignant tumors → evident metastasis & 20% → occult metastasis

Lymphatic spread (more common in **carcinomas**)

	Lymphatic permeation	Lymphatic Embolism
mechanism	Proliferation of tumor cells <u>inside lymph vessel</u> as a cord	movement of tumor emboli by lymph vessels into <u>lymph nodes</u> → found <u>subcapsular</u> → then destroy L.N.
Effects	-Lymphatic edema - Retrograde lymphatic spread (GIT & prostatic carcinoma → reach supra clav L.N. <u>Virchow's L.N.</u>)	-Regional LN: <u>large, firm, fixed</u> -Spread to other LNs -Late blood spread (?)

- **L.N. enlargement** in tumor is due to metastasis or Reactive Lymphadenitis and histocytosis caused by cancer products.
- GIT and some breast carcinomas → reach both ovaries by lymphatics Krukenberg tumor
- **Sentinel L.N.** is the 1st L.N. receiving metastasis

Hematogenous spread (early in **sarcomas**)

Mechanism:

- *Direct invasion of blood vessels (mostly veins) → tumor emboli covered by platelets as a thrombus → reach distant site → early blood spread (common in sarcoma)*
- *Lymphatic spread → late blood spread (carcinoma)*
- *Some carcinomas invade blood vessels: .Thyroid, HCC, RCC, prostatic*

Common Sites of metastasis:

- **Lung** Receive metastasis from tumors drained by systemic veins
e.g. RCC invades renal vein → inferior vena cava → right side of the heart
- **Liver** Receive metastasis from organs drained by portal vein (GIT)
- **Bone & Brain**

Organ Tropism

- Arrest of tumor emboli in vessels of specific organs by binding between adhesion molecules of tumor cells and specific receptors on target endothelium
- **Thyroid, Lung, breast, renal, & prostatic carcinomas** → bone metastasis
- **Sarcomas** → bone, Liver and Lung metastasis
- **Bronchial carcinoma** → Brain, liver and adrenal metastasis
- **Seminoma & RCC** → Lung metastasis

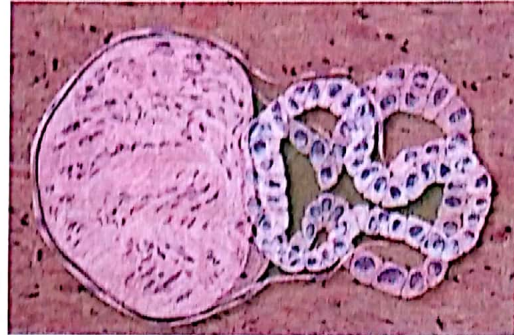


Spread through body cavities

- **Serous sac** : e.g. ovarian tumors → peritoneal , mesothelioma → pleural
- **CSF** : e.g. medulloblastoma → implanted in meninges

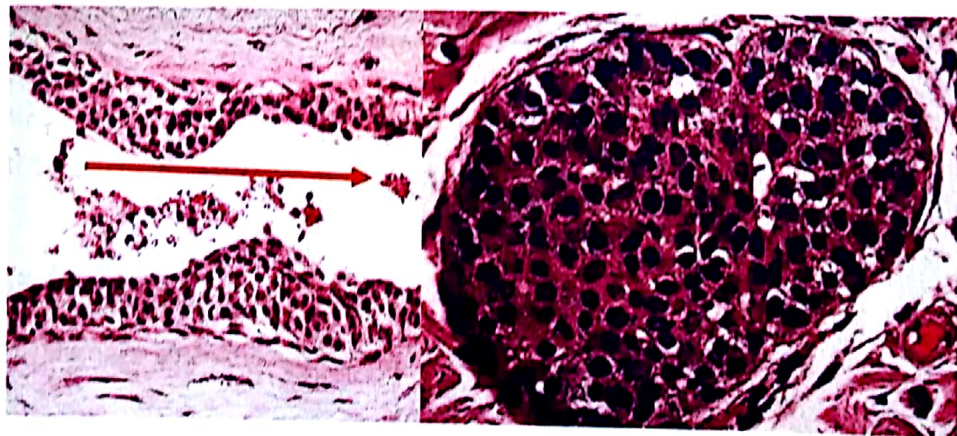
Perineural

Prostatic, Pancreatic, and Parotid adenoid cystic carcinoma → secrete **MMPs** →
Invade nerve → Pain. Poor prognosis



Intraepithelial

- **Duct carcinoma** may reach lobules through ducts
- **Endometrial carcinoma** reach ovaries through Fallopian tube
- **Renal Cell Carcinoma** reach urinary tract through ureter



Epithelial Tumors

Papilloma

Benign tumor of surface epithelium

Gross: papillae (*pedunculated – sessile*) - Single or multiple branching

Micro:

- **Core:** vascular fibrous tissue
- **Covered:** by proliferated epithelium
 - Squamous Cell Papilloma → covered by str. Squamous epith
 - Transitional Cell Papilloma → transitional
 - Columnar Cell Papilloma → columnar



Complications ulceration → bleeding & 2ry infection . Malignant transformation

Adenoma

Benign tumor of glandular epithelium

Sites

- Glands (*endocrine – exocrine*) : breast, thyroid, ovary, salivary...etc.
- GIT : Gastric ,intestinal, colonic

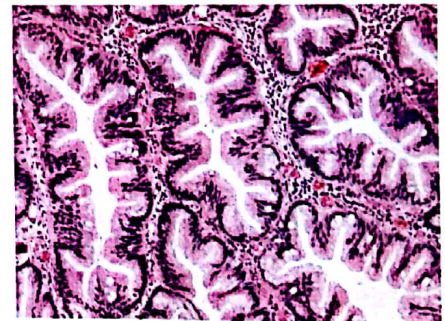
Gross

- Capsulated well defined in solid organs
- Polyp in GIT
- Cystic containing secretion, or papillary cystic

Micro: glandular tissue & stroma

Complications

- Secretion of hormones (*e.g. thyroid adenoma*)
- Malignant transformation (*GIT adenoma*)



Squamous cell carcinoma SCC

Malignant tumor of stratified Squamous epithelium

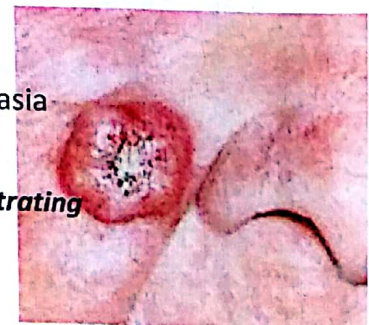
Sites: str. Sq. epithelium (*enumerate?*) - On top of squamous metaplasia

Gross:

Fungating, Ulcer: inverted edge , necrotic floor , hard base , **infiltrating**

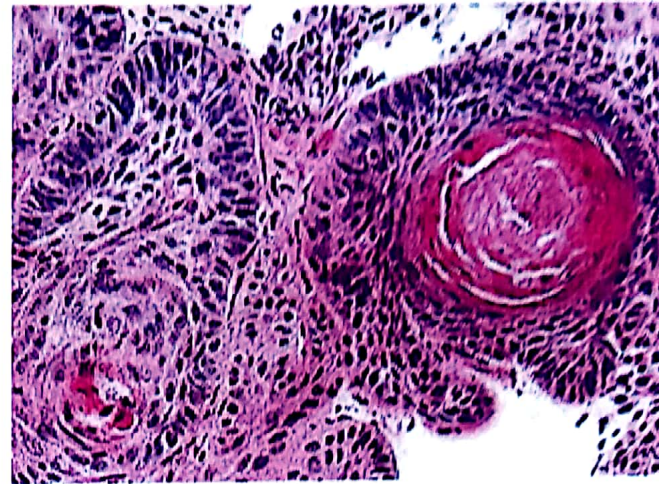
Micro:

- masses of malignant str. Sq. epith.
- variable in shape and size
- may show keratinized nests
- separated by stroma



Broder's grading:

- **Grade I:** 50% - 100% of masses → cell nest
- **Grade II:** 25% - 50% of masses → cell nest
- **Grade III:** less than 25% of masses → cell nest
- **Grade IV:** no cell nest



Carcinoma in situ (CIS)

Malignant epithelial changes, before invasion of basement membrane

Sites: glandular & surface epithelium: e.g. Breast, Bladder, Bronchi, Cervix, Skin... etc.

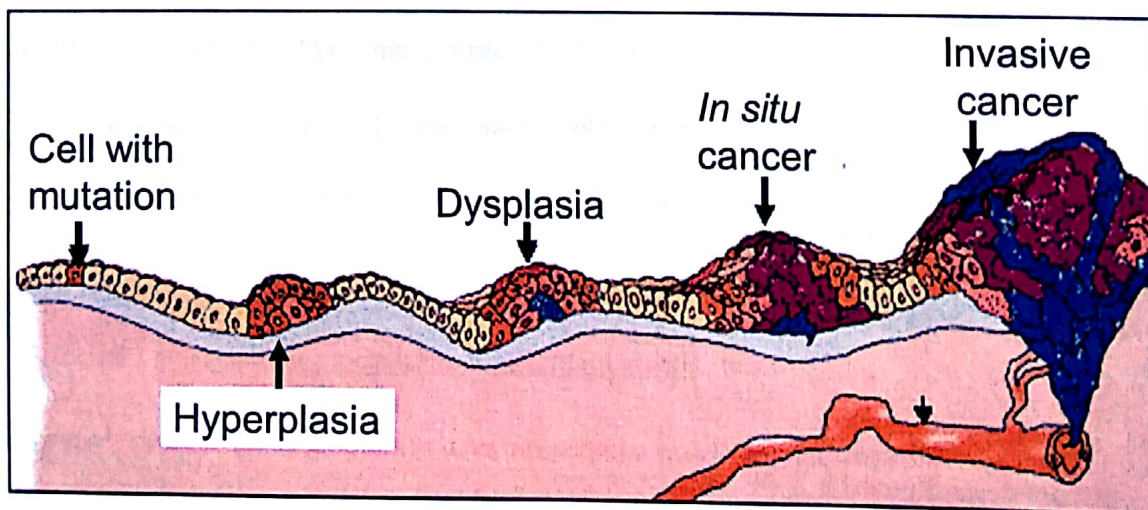
Micro:

Anaplasia (*enumerate..?*)

Loss of polarity (i.e. irregular arrangement of cells)

Basement membrane is intact

Fate: Invasive Carcinoma *after few years*



Basal cell carcinoma

Locally malignant 'Rodent ulcer'

Sites: Skin (upper part of the face, around the eye), neck, back, shoulder, hands

P.F. U.V. rays, Arsenic, radiation

Gross:

- Red nodule (sometimes brown)
- Ulcer: inverted rolled in edge – necrotic floor – fixed base

Micro:

Malignant Cells with scant cytoplasm:

- Forming basaloid masses
- Peripheral pallisading
- Surrounded by stroma
- Melanin pigment

Complications

Local invasion

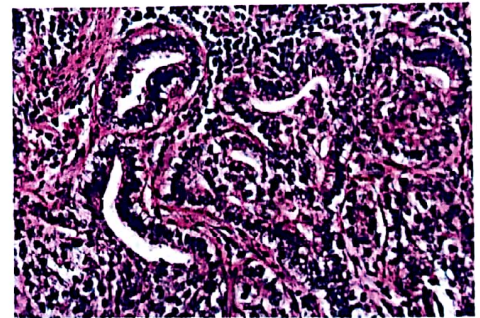
2ry infection of deep ulcers → lymphadenitis



Glandular-carcinoma

Adenocarcinoma 'Malignant tumor of glands'

- Well deffrentiated : malignant acini & stroma
- Poorly differentiated : malignant cells, less acini

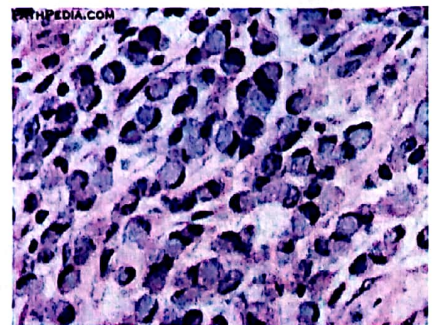


Mucoid : extracellular mucin lakes & malignant glands (e.g.GIT)

Signet ring: adeocarcinoma, with intracellular mucin (signet ring cell)

e.g. GIT

local spread is more aggressive



C.T. Tumors

Benign: e.g. Lipoma, fibroma

Gross: Capsulated well defined . **micro:** similar to origin

Malignant: Sarcomas

Haemangioma

The most common benign tumor

Sites: Subcutaneous – organs (*e.g. liver*)

Gross:

shape: irregular patch or swelling **color:** red, brown, blue

Micro:

- Vascular spaces lined with endothelium, containing RBCs
 - Small spaces in **Capillary hemangioma** (usually in skin)
 - Larger spaces in **Cavernous hemangioma** (skin and organs)
- Fibrous stroma between vessels



Lymphangioma

tumor forming vascular spaces containing lymph

Sites: Head , neck (**Cystic hygroma** of newborn) , Submucous (lip, and tongue) – organs (*e.g. liver, spleen*)

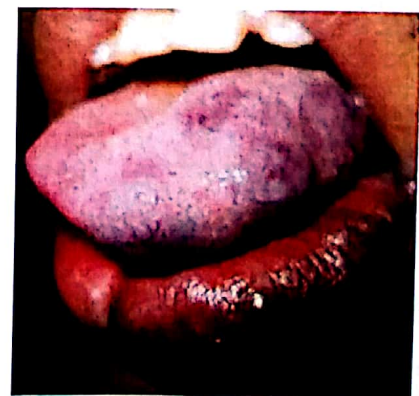
Gross:

shape: patch or swelling **capsule:** absent **color:** pale

Macro-glossia: enlarged tongue , macro-chelia: enlarged lips

Micro:

- Vascular spaces lined with endothelium, containing Lymph & lymphocytes
 - Small spaces in **Capillary lymphangioma**
 - Larger spaces in **Cavernous lymphangioma**
- Fibrous stroma between spaces



Nevus

Benign tumor of melanocytes

Gross: well defined Flat or elevated, brown or black

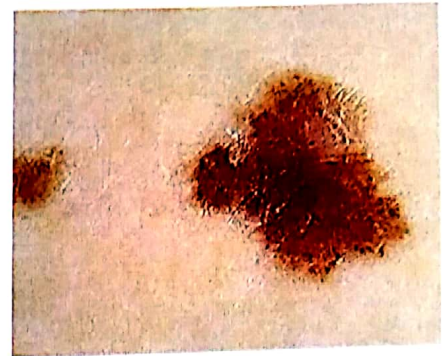
Microscopic Types: junctional – compound – intradermal

Melanoma

malignant tumor of melanocytes

Gross: nodule or malignant ulcer

Microscopic: malignant melanocytes, invading dermis
prognosis depends on depth of invasion



Teratoma

Composite tumor, forming ectodermal, mesodermal, and endodermal tissues, not related to site of origin

Origin:

- Embryonic rests: *present in midline & congenital*
- Germ cell → *gonadal & acquired*

Types:

- **Mature (benign)** well differentiated mixed tissue
- **Immature (malignant)** immature fetal tissue
- **Mature with malignant transformation** (e.g. mature with squamous cell carcinoma)
- **Mono-dermal** e.g. Struma-ovarii (normal thyroid tissue in ovary)



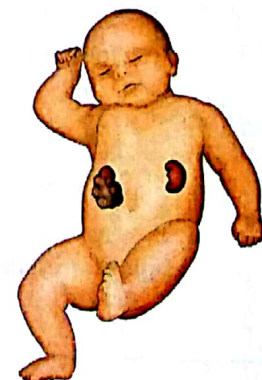
Embryonic tumors

Malignant tumor of embryonic tissue in children less than 5 years

Micro: Blastemal cells: small rounded or oval– dark nuclei

Types:

- Medulloblastoma (Cerebellum)
- Retinoblastoma (eye)
- Hepatoblastoma (liver)
- Neuroblastoma (adrenal medulla) the most common
- Nephroblastoma or Wilm's tumor (renal)



Hamartoma

Tumor-like mass of disorganized mature tissue

- Lung hamartoma: bronchi, vessels, and cartilage
- Liver hamartoma: Liver cells, bile ducts, & vessels

Choristoma: congenital ectopic tissue, e.g. pancreatic tissue in stomach

Locally malignant tumors

- Slower rate of growth
- Local invasion
- Rare distant spread
- Morphologically similar to malignant
- Better prognosis
- Includes:
 - Adamentenoma
 - Astrocytoma grade II
 - Basal cell carcinoma
 - Carcinoid
 - Desmoid tumor
 - Giant cell tumor (Osteoclastoma)

Grading of malignant tumor:

is microscopic evaluation of differentiation (similarity to origin) **I**: well differentiated
II: moderately differentiated **III**: poorly diff. **IV**: undifferentiated

Staging of malignant tumor: is evaluation of extension and spread, which is much more important than grading, and requires clinical and radiological investigations.

TNM system

T: tumor size & extent, **N**: number of affected LNs, **M**: distant blood metastasis

Tis: CIS T1: <2cm T2: 2-5 cm T3: 5-10cm T4: >10 cm

N0: no LN mets. N1: regional LN N2: extensive regional LN mets. N3: distant LN mets.

M0: no distant spread M1: distant blood spread

1-Pigmented malignant ulcer in the face could be one of the following (Except)

- a-Melanoma
- b-Basal cell carcinoma
- c- Hemangioma
- d-none

2- Staging of malignant tumors evaluates :

- a-differentiation
- b-necrosis
- c- a&b
- d- tumor extension

3- Signet ring carcinoma is a type of:

- a-Squamous cell carcinoma
- b-Adenocarcinoma
- c- Anaplastic carcinoma
- d- none of the above

4-Hamartoma is:

- a-Mixed germ cell tumor
- b-Malignant
- c-Tumor like developmental abnormality
- d-Locally malignant

5-Krukenberg tumor is:

- A-Peritoneal sarcoma
- b-Benign ovarian tumor
- c- Gastric carcinoma
- d- all of the above

6-All are embryonic tumors (except):

- a-Nephroblastoma
- b-Hepatoblastoma
- c- Embryonal rhabdomyosarcoma
- d- Teratoma

7-Virchow's lymph node , all of the following are true (except):

- a-induced by lymphatic embolism
- b-Left supraclavicular
- c- Gastric carcinoma is the origin
- d- Enlarged and fixed

8-Sarcoma is :

- a-Malignant of epithelium
- b-common to form malignant ulcer
- c- Highly vascular
- d- Common below 6 years

9-The following feature is characteristic for Basal cell carcinoma :

- a-Keratinized nests
- b-Blood metastasis is common
- c- Pallisading
- d- Skin is not the only site of origin

10-All The following tumors send metastasis (Except):

- a-Gastric carcinoma
- b-Adamantinoma
- c- Broncheogenic carcinoma
- d- Squamous cell carcinoma

11-The following are complications of benign tumors (except):

- a-hormonal imbalance
- b-Obstruction of tubes
- c- Hepatic metastasis
- d- Compression of vital organs

12-Struma ovarii is an ovarian tumor showing:

- A-Metastatic thyroid tissue
- b-normal thyroid tissue
- c- Immature teratoma
- d- Hamartoma

13-Broder's grading of Squamous cell carcinoma depends on:

- A-Invasion
- b-Keratinized cell nests
- c- Metastasis
- d- Inflammation

14- The most reliable prognostic factor of melanoma:

- A-Vertical thickness
- b-Radial diameter
- c- Darkness of color
- d- Anaplasia

15- Which of the following lesions is locally malignant:

- A-Giant cell tumor
- b-Endometrial hyperplasia
- c- Congenital nevus
- d- Hemangioma

True/ False:

- 1- Stage T2 N2 M0 has better prognosis than stage T3 N0 M0
- 2- Spindle cell sarcoma is a well differentiated sarcoma
- 3- Teratoma is epithelial in origin
- 4- Carcinoma in situ has local invasion without distant metastasis
- 5- The commonest site of cystadenoma is the breast
- 6- Adenocarcinoma has better prognosis than mucoid carcinoma
- 7- Papilloma is a benign capsulated tumor
- 8- Desmoplasia is an extensive fibrous reaction inside tumor
- 9- Mucoid carcinoma has better prognosis than adenocarcinoma
- 10- Prostatic carcinoma is painful due to perineural invasion
- 11- Virchow's L.N. is a result of retrograde lymphatic permeation
- 12- Some malignant tumors may reach the brain without lung metastasis
- 13- Krukenberg tumor is a bilateral ovarian metastasis of gastric carcinoma
- 14- Sarcomas are commonly sending metastasis to L.N.s
- 15- Malignant ulcer has undermined edges & smooth floor